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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/617,569	07/17/2000	Petrus W. Roelvink	204133	7936

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EXAMINER

FOLEY, SHANON A

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 03/11/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/617,569

Applicant(s)

ROELVINK ET AL.

Examiner

Shanon Foley

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6,8-19,21-32,40 and 43-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6,8-19,21-32,40 and 43-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

In paper no. 13, applicant cancelled claims 7, 20, 41, 42, amended claims 1, 8, 9, 26 and 40 and added new claims 44-51. Claims 1-6, 8-19, 21-32, 40 and 43-51 are under consideration.

Request for Continued Examination

The request filed on 6/18/02 for a Request for Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/617,569 is acceptable and a RCE has been established. An action on the RCE follows.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6, 8-17, 19, 21-24, 26-31, 40, 43, 44, 46, 48 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wickham et al. (US 5,846,782) and Kikuchi et al. (Human Gene Therapy. 1999; 10: 1375-1387).

The claims are drawn to a complex comprising a virion that has a non-native ligand that recognizes an epitope on an immune effector cell, an RGD motif, and a non-native antigen on the surface. The non-native antigen is a gene product from a pathogen or a malignant cell and the ligand recognizes CD-40. The virion comprises a chimeric protein where the first protein is from an adenovirus capsid protein and the second domain is a ligand, and elicits less specific immunogenicity than the wild-type virus. The complex is inoculated by a pharmaceutical carrier to elicit an immune response.

Art Unit: 1648

Wickham et al. teach a recombinant adenovirus that has a chimeric adenovirus fiber protein comprising an RGD motif, see claims 1-3, 8, 19, 20, and 24; column 6, lines 28-53 and column 9, lines 29-45. Wickham et al. also teach the incorporation of a passenger gene elicits a strong immune response resulting in a therapeutic effect, see column 14, lines 37-59, column 19, lines 19-38, and column 20, lines 12-26. Wickham et al. also describes gene delivery mediated by adenovirus vectors having insertions of various peptide motifs of the adenovirus fiber protein and delivery of the recombinant vector into liposomes, see column 18, line 40. Wickham et al. do not teach expressing CD-40 ligand on the surface of the adenovirus.

However, Kikuchi et al. teach a recombinant adenovirus expressing a CD-40 ligand, see "Adenovirus vectors" on page 1376.

One of ordinary skill in the art at the time the invention was made would have been motivated to express a CD-40 ligand on the adenovirus of Wickham et al. to induce antigen-presenting cells to present antigens to the cellular immune system. Although neither reference expressly teaches expressing a second antigen on the adenovirus surface, one of ordinary skill in the art at the time the invention was made would have been motivated to express an antigen on the surface of the adenovirus to induce a specific immune response against a particular antigen.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because both Kikuchi et al. and Wickham et al. use adenovirus to express recombinant ligands on an adenovirus vector surface. Also, Wickham et al. teach that adenovirus vectors possess substantial carrying capacity for multiple heterologous gene expression, see column 1, lines 25-29. Therefore, the invention as a

Art Unit: 1648

whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 18, 25, 32 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wickham et al. and Kikuchi et al. as applied to claims 1-6, 8-17, 19, 21-24, 26-31, 40, 43, 44, 46, 48 and 50 above, and further in view of Janeway et al. (1997. Immunobiology. 3rd edition. Garland Publishing Inc. Page 7:27).

The claims are drawn to at least one polypeptide being a cytokine.

See the teachings of Wickham et al. and Kikuchi et al. Neither reference teaches incorporating a cytokine into the adenovirus complex.

However, Janeway et al. teach a number of cytokines and their effect on the immune response. Figure 7.31 on page 7:27 teaches that INF- γ activates MHC classes I and II. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate INF- γ into the immune complex as the second non-native antigen into the complex in order to achieve a natural immune response by activating MHC I and II. In addition, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation in producing the claimed invention because of the natural characteristic of the interferon to invoke a strong immune response. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant argues that the Office fails to provide any objective evidence to motivate the ordinary artisan to combine the references.

Art Unit: 1648

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Wickham et al. and Kikuchi et al. teach recombinant adenoviruses that redirect native viral tropism and induce an antigen-specific immune response by expressing various recombinant ligands on the surface of an adenovirus vector. Although neither reference explicitly teaches expression of an antigen on surface of the chimeric adenovirus, Wickham et al. teach that adenoviruses have the capacity to express a wide range of recombinant genes. The reference also teaches expressing passenger or therapeutic genes in chimeric adenoviruses. One of ordinary skill in the art at the time the invention was made would have been motivated to express an antigen to induce a specific immune response against the particular antigen by expressing the antigen on the adenovirus surface. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because Wickham et al. and Kikuchi et al. teach how to redirect the immune response to a chimeric adenovirus expressing a chimeric fiber protein.

Neither reference teaches expression of a cytokine. However, Janeway et al. do. One of ordinary skill in the art at the time the invention was made would have been motivated to express interferon in the recombinant adenovirus of Wickham et al. and Kikuchi et al. to ensure induction of a strong immune response in tumor cells. One of ordinary skill in the art at the time

Art Unit: 1648

the invention was made would have had a reasonable expectation for producing the claimed invention because Kikuchi et al. teach that antigen-specific T cell responses are important for anti-tumor immune responses and Janeway et al. teach that interferon induces MHC I and MHC II immune responses. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 47, 49 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wickham et al. and Kikuchi et al. as applied to claims 1-6, 8-17, 19, 21-24, 26-31, 40, 43, 44, 46, 48 and 50 above, and further in view of Ashkar et al. (Science. February 4, 2000; 287: 861-864).

The claims are drawn to at least one polypeptide being osteopontin.

See the teachings of Wickham et al. and Kikuchi et al. above. Neither reference teaches osteopontin.

However, Ashkar et al. teach that osteopontin stimulates IL-12 expression, see the abstract.

One of ordinary skill in the art at the time the invention was made would have been motivated to express osteopontin in the recombinant adenovirus of Wickham et al. and Kikuchi et al. to induce IL-12 production because Ashkar et al. teach that cell-mediated immunity provides protective immunity against cellular pathogens. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the claimed invention because Wickham et al. teach that adenoviruses have the capacity to express a wide range of recombinant genes, Kikuchi et al. teach that antigen-specific T cell responses are important for anti-tumor immune responses and both Wickham et al. and Kikuchi et al. express

Art Unit: 1648


various recombinant ligands on the surface of an adenovirus vector. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

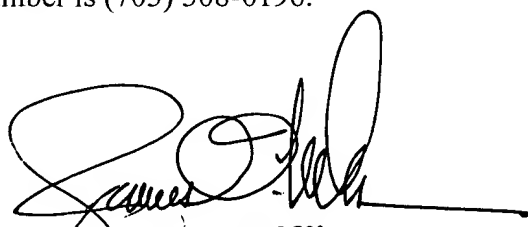
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


Shanon Foley
March 10, 2003


JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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